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QUERY CONTROL FORM				RTIS USE ONLY	
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JACKET			
a. Serial No.	f. Foreign Priority	k. Print Claim(s)	p. PTO-1449
b. Applicant(s)	g. Disclaimer	l. Print Fig.	q. PTOL-85b
c. Continuing Data	h. Microfiche Appendix	m. Searched Column	r. Abstract
d. PCT	i. Title	n. PTO-270/328	s. Sheets/Figs
e. Domestic Priority	j. Claims Allowed	o. PTO-892	t. Other

SPECIFICATION

a. Page Missing
b. Text Continuity
c. Holes through Data
d. Other Missing Text
e. Illegible Text
f. Duplicate Text
g. Brief Description
h. Sequence Listing
i. Appendix
j. Amendments
k. Other

CLAIMS

a. Claim(s) Missing
b. Improper Dependency
c. Duplicate Numbers
d. Incorrect Numbering
e. Index Disagrees
f. Punctuation
g. Amendments
h. Bracketing
i. Missing Text
j. Duplicate Text
k. Other

MESSAGE

Amendment A8 is not clear where its supposed to end. Copies provided for reference Please advise.

Thank you,

initials LR

RESPONSE

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E-5 (Rev. 10/01/02)

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sulfonate, hydroxycarbonylalkyl (carboxyalkyl), hydroxyalkylaminocarbonyl, cyano, amino, heterocyclylalkylamino, carboxyalkylamino, carboxyalkenyl, alkoxycarbonylalkenyl, heterocyclylalkylaminocarbonyl, and "*trans*-cinnamide" substituents, where the alkyl, aryl, and heterocyclyl groups alone, or as joined with another radical, can be optionally substituted with one or more than one substituent as described herein.

Beginning on page 15, line 18 and ending on page 16, line 13:

The terms "heterocycle" or "heterocyclyl" represent a 4-, 5-, 6- or 7-membered ring containing one, two or three heteroatoms independently selected from the group consisting of nitrogen, oxygen and sulfur. The 4- and 5-membered rings have zero to two double bonds and the 6- and 7-membered rings have zero to three double bonds. The term "heterocycle" or "heterocyclic" as used herein additionally refers to bicyclic, tricyclic and tetracyclic groups in which any of the above heterocyclic rings is fused to

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one or two rings independently selected from an aryl ring, a cyclohexane ring, a cyclohexene ring, a cyclopentane ring, a cyclopentene ring or another monocyclic heterocyclic ring. Heterocycles include acridinyl, benzimidazolyl, benzofuryl, benzothiazolyl, benzothienyl, benzoxazolyl, biotinyl, cinnolinyl, dihydrofuryl, dihydroindolyl, dihydropyranyl, dihydrothienyl, dithiazolyl, furyl, homopiperidinyl, imidazolidinyl, imidazolinyl, imidazolyl, indolyl, isoquinolyl, isothiazolidinyl, isothiazolyl, isoxazolidinyl, isoxazolyl, morpholinyl, oxadiazolyl, oxazolidinyl, oxazolyl, piperazinyl, piperidinyl, pyranyl, pyrazolidinyl, pyrazinyl, pyrazolyl, pyrazolinyl, pyridazinyl, pyridyl, pyrimidinyl, pyrimidyl, pyrrolidinyl, oxopyrrolidinyl, pyrrolinyl, pyrrolyl, quinolinyl, quinoxaloyl, tetrahydrofuryl, tetrahydroisoquinolyl, tetrahydroquinolyl, tetrazolyl, thiadiazolyl, thiazolidinyl, thiazolyl, thienyl, thiomorpholinyl, triazolyl, dioxaspirodecanyl, dioxotriazaspirodecanyl, and the like.

Beginning on page 16, line 18 and ending on page 19, line 5:

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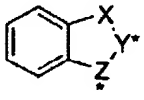
V unclear

Heterocyclics also include compounds of the formula  where X* and Z* are independently selected from -CH_2-, -CH_2NH-, -CH_2O-, -NH- and -O-, with the proviso that at least one of X* and Z* is not –CH_2-, and Y* is selected from -C(O)- and -$(C(R'')_2)_v$ -, where R'' is hydrogen or alkyl of one to four carbons, and v is 1-3. These heterocycles include 1,3-benzodioxolyl, 1,4-benzodioxanyl, 2,3-dihydro-1H-benzimidazol-2-one and the like. The heterocycle groups of this invention, unless otherwise specified, can be optionally substituted with one or more than one substituent, including but not limited to, alkanoyl, alkanoylamino, alkanoylaminoalkyl, alkanoyloxy, alkanoyloxyalkyl, alkenoxycarbonyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, alkoxyalkylaminocarbonyl, alkoxycarbonyl, alkoxycarbonylalkenyl, alkoxycarbonylalkyl, alkyl, alkyl(alkoxycarbonylalkyl)aminoalkyl, alkylsulfanyl, alkylsulfonyl, alkylsulfonylaminocarbonyl, amino, aminoalkanoyl, aminoalkyl, aminocarbonyl, aryl, arylalkoxycarbonyl, aryl(carboxy)alkylaminocarbonyl arylsulfonylaminocarbonyl, carboxaldehyde, carboxaldehyde hydrazone, carboxamide, carboxamidoalkyl, carboxy, carboxyalkoxy, carboxyalkenyl, carboxyalkyl, carboxyalkylamino, carboxyalkylaminocarbonyl, carboxycarbonyl, carboxycycloalkoxy, carboxythioalkoxy, cyano, cycloalkyl, haloalkyl, halogen, unsubstituted heterocyclyl, substituted heterocyclyl, unsubstituted heterocyclylalkyl, substituted heterocyclylalkylamino, heterocyclylalkylaminocarbonyl, heterocyclylcarbonyl, heterocyclylsulfonylaminocarbonyl, hydroxy, hydroxyalkanoyl, hydroxyalkoxyalkyl, hydroxyalkyl, hydroxyalkylaminocarbonyl, hydroxyaminocarbonyl, hydroxy(carboxy)alkylaminocarbonyl, hydroxy(carboxy)alkylcarbonyl, hydroxycarbonylalkyl(carboxyalkyl), sulfonate, unsubstituted tetrazolyl, substituted tetrazolyl, sulfoalkylaminocarbonyl, and "*trans*-cinnamide," substituents where the alkyl, aryl, and heterocyclyl groups alone, or as joined with another radical, can be optionally substituted with one or more than one substituent as described herein.

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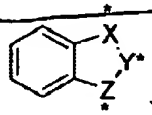
Beginning on page 18, line 18 and ending on page 19, line 2:

tricyclic and tetracyclic groups in which any of the above heterocyclic rings is fused to one or two rings independently selected from an aryl ring, a cyclohexane ring, a cyclohexene ring, a cyclopentane ring, a cyclopentene ring or another monocyclic heterocyclic ring. Heterocycles include acridinyl, benzimidazolyl, benzofuryl, benzothiazolyl, benzothienyl, benzoxazolyl, biotinyl, cinnolinyl, dihydrofuryl, dihydroindolyl, dihydropyranyl, dihydrothienyl, dithiazolyl, furyl, homopiperidinyl, imidazolidinyl, imidazolinyl, imidazolyl, indolyl, isoquinolyl, isothiazolidinyl, isothiazolyl, isoxazolidinyl, isoxazolyl, morpholinyl, oxadiazolyl, oxazolidinyl, oxazolyl, piperazinyl, piperidinyl, pyranyl, pyrazolidinyl, pyrazinyl, pyrazolyl, pyrazolinyl, pyridazinyl, pyridyl, pyrimidinyl, pyrimidyl, pyrrolidinyl, pyrrolidin-2-onyl, pyrrolinyl, pyrrolyl, quinolinyl, quinoxaloyl, tetrahydrofuryl, tetrahydroisoquinolyl, tetrahydroquinolyl, tetrazolyl, thiadiazolyl, thiazolidinyl, thiazolyl, thienyl, thiomorpholinyl, triazolyl, and the like.

Heterocyclics also include bridged bicyclic groups where a monocyclic heterocyclic group is bridged by an alkylene group such as

, and the like.

Heterocyclics also include compounds of the formula  where X* and Z* are independently selected from $-CH_2-$, $-CH_2NH-$, $-CH_2O-$, -NH- and -O-, with the proviso that at least one of X* and Z* is not $-CH_2-$, and Y* is selected from

-C(O)- and -(C(R")2)v -, where R" is hydrogen or alkyl of one to four carbons, and v is 1-3. These heterocycles include 1,3-benzodioxolyl, 1,4-benzodioxanyl, 1,3-benzimidazol-2-one and the like. The heterocycle groups of this invention can be optionally substituted with alkoxy, alkyl, halogen, hydroxy, carboxy, carboxyalkyl, or alkoxycarbonyl substituents.

The term "heterocyclylalkyl" as used herein refers to an heterocyclic group attached to the parent molecular group through an alkyl group.

The term "heterocyclylalkylamino" as used herein refers to an heterocyclylalkyl group attached to the parent molecular group through an amino group.

The term "heterocyclylalkylaminocarbonyl" as used herein refers to a heterocyclylalkylamino group attached to the parent molecular group through a carbonyl group.

The term "heterocyclylamino" as used herein refers to a heterocyclyl group attached to the parent molecular group through a amino group.

The term "heterocyclylcarbonyl" as used herein refers to a heterocyclyl group attached to the parent molecular group through a carbonyl group.

The term "heterocyclylsulfonyl" as used herein refers to a heterocyclyl radical attached to the parent molecular group through an $-SO_2-$ group.

The term "heterocyclylsulfonylaminocarbonyl" as used herein refers to a heterocyclylsulfonyl group attached to the parent molecular group through an aminocarbonyl group.

The term "hydroxyalkanoyl" as used herein refers to an hydroxy radical attached to the parent molecular group through an alkanoyl group.

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The term "hydroxyalkoxy" as used herein refers to an hydroxy radical attached to the parent molecular group through an alkoxy group.

The term "hydroxyalkoxyalkyl" as used herein refers to an hydroxyalkoxy group attached to the parent molecular group through an alkyl group.

The term "hydroxyalkyl" as used herein refers to an hydroxy radical attached to the parent molecular group through an alkyl group.

The term "hydroxyalkylaminocarbonyl" as used herein refers to an hydroxyalkyl group attached to the parent molecular group through an aminocarbonyl group.

The term "perfluoroalkyl" as used herein refers to an alkyl group in which all of the hydrogen atoms have been replaced by fluoride atoms.

The term "phenyl" as used herein refers to a monocyclic carbocyclic ring system having one aromatic ring. The phenyl group can also be fused to a cyclohexane or cyclopentane ring. The phenyl groups of this invention can be optionally substituted with alkyl, halogen, hydroxy or alkoxy substituents.

The term "pharmaceutically-acceptable prodrugs" as used herein represents those prodrugs of the compounds of the present invention which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and lower animals with undue toxicity, irritation, allergic response, and the like,

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commensurate with a reasonable benefit/risk ratio, and effective for their intended use, as well as the zwitterionic forms, where possible, of the compounds of the invention.

The term "prodrug," as used herein, represents compounds which are rapidly transformed *in vivo* to the parent compound of the above formula, for example, by hydrolysis in blood. A thorough discussion is provided in T. Higuchi and V. Stella, Pro-drugs as Novel Delivery Systems, Vol. 14 of the A.C.S. Symposium Series, and in Edward B. Roche, ed., Bioreversible Carriers in Drug Design, American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated herein by reference.

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The term "sulfonate" as used herein refers to the radical $-SO_3H$

The term "tetrazole" or "tetrazolyl" as used herein refers to the heterocyclic radical $-CN_4H$.

The term "thioalkoxy" as used herein refers to an alkyl group attached to the parent molecular group through a sulfur atom.

Compounds of the present invention can exist as stereoisomers wherein asymmetric or chiral centers are present. These compounds are designated by the symbols "R" or "S," depending on the configuration of substituents around the chiral carbon atom. The present invention contemplates various stereoisomers and mixtures thereof. Stereoisomers include enantiomers and diastereomers, and mixtures of enantiomers or diastereomers are designated ($\pm$). Individual stereoisomers of compounds of the present invention can be prepared synthetically from commercially available starting materials which contain asymmetric or chiral centers or by